



Contemporary Management of Acute Biliary Pancreatitis

Akut Biliyer Pankreatitin Güncel Yönetimi

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Özet

Akut biliyer pankreatit, en yaygın akut pankreatit nedenlerindedir. Safra taşları, safra çamuru, özellikle nedeni saptanamayanlarda mikrolityazis pankreatit nedeni olabilmektedir. Akut biliyer pankreatit konusu literatürde çok tartışmalı yönleri olan ve sınıflandırma ve klavuzları çok hızlı değişen bir konudur. Akut pankreatit ile ilgili tanımlamaların ve klasifikasyonların yapıldığı Atlanta kriterleri yenilenecek 2013 yılında yayınlanmıştır. Akut biliyer pankreatitte çok kolay tedavi edilebilen hafif şekline kadar geniş bir spectrum vardır. Bu hastalığın patogenezi tam olarak aydınlatılmamış ve çeşitli teoriler ileri sürülmüştür. Gerek tanı gerekse ağırlık derecesini tahmin etmek için protomiks gibi yeni laboratuvar yöntemleri ve skorlama sistemleri önerilmiş ve bunlarla ilgili çalışmalar devam etmektedir. ERCP, ES, MRCP, EUS gibi teknolojik gelişmelerle ilişkili yeni tedavi yaklaşımları önerilmektedir.

Anahtar Kelimeler

Akut Biliyer Pankreatit; Tanı; Ağırlığıöngörme; Tedavi

Abstract

Acute biliary pancreatitis is one of the major causes of acute pancreatitis. Gallstones, biliary sludge and microlithiasis, especially in pancreatitis without detectable reason, can be the cause of acute pancreatitis. Acute biliary pancreatitis has many controversions in the literature, and its classification and guidelines are being updated very frequently. Atlanta classifications which determine the definitions and guidelines about acute pancreatitis were renewed and published in 2013. It has various clinical aspects, ranging from a mild form which is easily treated, to a severe form that causes complications leading to mortality. The pathogenesis of this disease has not been fully elucidated and several theories have been suggested. New scoring systems and laboratory methods such as proteomics have been suggested for both diagnosis and to predict disease severity, and research on these topics is still in progress. Novel therapeutic approaches with technological developments such as ERCP, ES, MRCP, and EUS are also suggested.

Keywords

Acute Biliary Pancreatitis; Diagnosis; Predictors Severity; Treatment

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Introduction

Acute pancreatitis is the reversible paranchymal injury related to the pancreatic inflammation, which can be observed in local and distant extrapancreatic tissues[1]. Gallstones are among the major causes. Small gallstones and sludge are the most frequent acute pancreatitis causes in the Western world[2,3]. If any etiological factor cannot be detected, the disease is referred to as idiopathic acute pancreatitis. However, some of these cases can be related to microlithiasis[4].

Acute pancreatitis caused by gallstones was defined in 1901 by Eugene Opie with the common canal theory. Gallstones fall to the duodenum in 70% of the cases[5,6]. However, this situation may differ with the severity of acute pancreatitis, duration of the temporary obstruction in the middle canal or its persistence. In this review, diagnosis, prediction criteria for pancreatitis severity, scoring systems and treatment approaches for acute biliary pancreatitis (ABP), which is among the most frequently observed acute pancreatitis.

Diagnosis

The diagnosis of acute pancreatitis is made if at least two of the following three criteria are met: 1-Acute abdominal pain 2- Elevated pancreatic enzyme levels in blood, urine or acidic liquid 3- Abnormal imaging findings in pancreas that are related with acute pancreatitis. If the diagnosis is made on this basis, other pancreatic diseases and acute abdomen reasons can be ruled out[7]. Distinguishing between acute biliary pancreatitis and other causes of acute pancreatitis is important for disease management and prognosis.

Symptoms and signs

Various clinical symptoms and signs, including abdominal pain, nausea, vomiting, ileus, subileus, reduced bowel sound, fever, jaundice, pain extending to the dorsum, shock, anorexia, abdominal muscular rigidity and neurological symptoms can be observed in acute pancreatitis.

Acute pancreatitis sometimes cause color change in the skin in side abdominal wall (Grey Turner's sign), around the belly (Cullen's sign), or on the lower part of inguinal ligament (Fox's sign)[7].

Abdominal pain is observed in approximately 95% of the cases. In patients with biliary pancreatitis, pain is localized more on the right upper quadrant[8,9]. The presence of gallstones in patient history helps to consider ABP in the diagnosis. Vomiting is associated with peripancreatic inflammation extending to the posterior gastric wall and local/generalized ileus[9].

Other frequent symptoms and signs in patients with acute pancreatitis include pain extending to the dorsum, loss of appetite, jaundice, muscular defence, meteorism and hematemesis[10].

Current diagnostic biomarkers

Serum amilase and lipase levels are standard blood tests. Serum amilase levels increase rapidly in the onset of acute pancreatitis (3-6 hours), persist for 3-5 days[11]. Moreover, amilase levels may increase due to other reasons except acute pancreatitis, such as perforated peptic ulcer, perforated/obstructed bowel, mesenteric infarction, trauma, salivary diseases, cholecystitis and peritonitis[12]. Lipase values are more sensitive compared to amilase. In addition to these, hyperglycemia, hypocalcemia, leukocytosis, anemia, moderate hyperbilirubinemia and an increase in liver enzyme levels can be observed.

In 2007, American Academy of Family Physicians emphasized to use amilase and lipase values, whole blood count, blood urea,

creatinine, glucose, calcium, triglyceride, urine examination and arterial blood gas in the diagnosis and treatment of acute pancreatitis. Additional research biomarkers may include trypsinogen activation peptide (TAP), CRP, procalcitonin, phospholipase A2 and the cytokines interleukin-6 and interleukin-8[13].

While several prognostic biomarkers, including procalcitonin, serum interleukin-6, interleukin-8, polymorphonuclear elastase and serum CRP, have been investigated, the research on diagnostic test had less efficiency[14,15]. Certain interesting biomarkers have been defined; yet, when compared with lipase, their lower accuracy and requirement for slow techniques which are not suitable for clinical laboratories and fast diagnosis prevented their widespread use. Phospholipase A2, pancreatic elastase, urinetrypsinogen activated protein (TAP), carboxypeptidase B (CAPB), activation peptide of carboxypeptidase B (CAPAP), trypsin-2-alpha1 antitrypsin complex (trypsin-2-AAT) and circulating (cell-free) DNA are examples for such laboratory biomarkers which did not find widespread use[12].

As a novel approach, "proteomics" studies have increasing importance and these studies accelerated following the completion of the human genome project, and found a widespread area of application. Despite the fact that genomics has been the dominant research area in biomedical studies in recent years, research on proteomics is rapidly spreading among scientific research groups and clinical research laboratories[16]. Currently, there are ongoing proteomic studies on acute pancreatitis, and they are expected to have key positions to determine both diagnosis and prognosis. There are ongoing proteomics studies on novel potential biomarkers, including protein disulfide isomerase related protein, dnaK-type molecular chaperone hsp72-ps1, mitochondrial glutamate dehydrogenase, similar to chaperonin containing TCP-1 β subunit, RuvB-like protein1, heterogeneous nuclear ribonucleoprotein H1, aldehyde reductase1, triosephosphate isomerase1, peroxiredoxin2, heat shock protein90, mitochondrial ATP synthase β chain precursor, tubulin β chain, 3-mercaptopyruvate sulfurtransferase and mitochondrial ATP synthase subunit D[12].

Imaging finding of ABP

CT is the major imaging method to evaluate acute pancreatitis. It is important to detect the disease and to evaluate its severity. What is more important, probably, is that CT is considerably useful to evaluate situations presented with clinical symptoms similar to acute pancreatitis, such as duodenal ulcer perforation, ruptured aortic aneurism and mesenteric ischemia[17,18]. Ultrasonography (US) is a relatively sensitive method to evaluate gallbladder and biliary tracts, and its feasibility and mobility ensures point-of-care evaluation. However, the fact that the distal parts of the coledoc cannot be evaluated due to bowel gas superposition constitutes a disadvantage of this method. Stones causing acute pancreatitis are generally smaller than 5mm[19]. Magnetic resonance imaging (MRI) is considerably successful to show biliary tracts and pancreatic ducts that contain stable fluid. These sequences can be used to perform magnetic resonance cholangiopancreatography (MRCP), and it is the non-invasive alternative to endoscopic retrograde cholangiopancreatography (ERCP). For common bile duct stones, MRCP's sensitivity and specificity is above 90%[20].

Identification of acute biliary pancreatitis

The first recommendation in ABP definition is to inspect the presence of stones in the gallbladder and/or coledoc using US.

The sensitivity of US to detect gallstones exceeds 95% in uncomplicated cases. However, in cases of acute pancreatitis, the sensitivity is only 67-78% due to ileus and bowel distention. Furthermore, the sensitivity ranges between 25-90% for detecting common bile duct stones. Detecting especially small stones that cause pancreatitis, even the probability of these stones passing to the intestine makes the detection of common bile duct stones using US complicated.

Alanine aminotransferase (ALT), elevated γ -glutamyltransferase (GGT) and bilirubin also leads to a suspicion of ABP, but it should be noted that ABP may be present although these parameters have normal levels. If gallstones are not detected by US, and presence of jaundice and elevated biochemical parameters indicate ABP. MRCP and endoluminal US(EUS), which have higher sensitivity and specificity, should be performed. MRCP has high sensitivity(84-95%) and specificity (96-100%) to detect common bile duct stones. EUS, similar to MRCP, has high degree to detect stones in the main biliary tracts[21,22].

Pathophysiology

While only 3-7% of the patients who have gallstone in the gallbladder are known to develop pancreatitis, clearing residual gallstones by cholecystectomy or ERCP after pancreatitis prevents recurrent pancreatitis attacks. When left untreated, the recurrence rate of gallstone pancreatitis ranges between 32-61%[23]. Sludge that causes stasis in biliary flow is among the causes of acute pancreatitis. Sludge consisting of cholesterol crystals and calcium granules may include stones smaller than 5mm. It forms a dense layer in the gallbladder. Behaving similarly to gallstones, it may cause acute pancreatitis and similarly, cleaning coledoc using cholecystectomy and ERCP may prevent recurrent pancreatitis attacks[24,25].

Experimental studies have demonstrated that biliary reflux was not a necessity for acute pancreatitis development, and pancreatitis may develop as a result of pancreatic duct obstruction[26]. According to another theory, insufficient inhibition of intracellular trypsinogen activation leads to an increase in pressure in the pancreatic duct when exocrine pancreas is hyperstimulated, active trypsin reflux is elevated and thereby, pancreatic injury develops[27].

Biliary tract stones that cause pancreatitis may not be present radiologically in all cases. The stone might have passed the Oddi sphincter or it could be really small, referred to as microlithiasis, which cannot be presented with conventional abdominal US[28]. Microlithiasis condition may cause recurrent pancreatitis as the migration of the stones is easy. Moreover, hepatic transaminase levels are also normal in 15-20% of these cases[29].

In 1901, Eugene Opie proposed the "common channel theory"[5]. Main biliary tract and pancreatic duct open to the duodenum with a common canal, and a gallstone localized to ampulla Vater causes an obstruction at this location, leading to gallbladder reflux and pancreatitis[3]. Acosta and Ledesma[30] suggested that biliary reflux associated with the temporary obstruction in papilla, which is caused by the migration of gallstones to the duodenum, might cause pancreatitis. In the end, biliary reflux due to obstruction or gallbladder itself can damage the protective barrier in the pancreatic cells, or activate pancreatic enzymes via indirect mechanisms to cause pancreatitis.

Duodenal reflux theory is defined as the damage exerted by gallstones on the muscular layer of oddi sphincter during their migration to the duodenum, and subsequent retrograde flow of the duodenal content into the pancreatic duct[31]. According to

another theory[1], the increase in pancreatic permeability in the pancreatic duct due to the obstruction that is caused by the stones, can lead to pancreatic enzymes to overcome the protective barrier to cause pancreatitis.

Inflammation is generally limited to a localized zone of injury. However, in certain cases, the severity of inflammation turns into systemic inflammatory response syndrome(SIRS) due to the overactivation of the inflammatory cascade which is regulated by cytokines, immunocytes and the complement system. Inflammatory cytokines cause macrophages to migrate to distant organs, such as lungs or liver. Immunocytes stimulated by the cytokines released from macrophages secrete more cytokines, free radical and nitric oxide. Certain cytokines and proteins that play roles in disease progression, including IL-1, IL-6, IL-8, IL-10, TNF- α , monocyte chemoattractant protein, macrophage inhibitor factor, C-reactive protein and serum amyloid A, are important for monitoring the disease[1].

Prediction of Disease Severity

The severity of the disease is evaluated by combining clinical and laboratory findings, and using Atlanta criteria, Ranson criteria and acute physiology and chronic health evaluation II(APACHE II)scoring system. CT severity index developed by Balthazar et al. is used to evaluate the disease severity[32]. In this index, necrosis and presence, amount and extension of fluid collections are evaluated and a patient is given a score.

Serum C-reactive protein(CRP)(cut-off >150)is suggested to evaluate the severity of acute pancreatitis 48-72 hours after its onset[12].

Scoring systems including multiple criteria have been defined 30 years ago to predict the disease prognosis and severity. Among these systems are Bank, Agarwal-Pitchumoni, Ranson, Glasgow (Imrie), APACHE II, BISAP, Balthazar, and Atlanta criteria.

In addition, Japanese clinical practice guidelines for acute pancreatitis was published in 2003 in Japan, and in 2006 in English. Later on, the Japanese Ministry of Health, Labour and Welfare developed novel diagnostic criteria in 2008 and revised the acute pancreatitis severity scoring system[33].

Ranson score

Ranson criteria, which is a pancreatitis-specific scoring system, is based on the evaluation of certain clinical and laboratory findings at the time of admission and at 48th hour. It consists of a total of 11 parameters, 5 of which are measured at the time of admission, and 6 of which are measured within the first 48 hours[33]. It is modified for ABP(Table)[34,35]. Glasgow prognostic criteria including 8 parameters was defined by Imrie.

APACHE classification

APACHE criteria, which consisted of 34 criteria, was defined in 1981. However, due to its impractical use, it was modified as APACHE II, which included 12 criteria, in 1985. The sensitivity of this scoring system to determine pancreatitis severity is 75%, whereas it has a specificity of 92%[36,37].

APACHE III consisting of 18 criteria was defined in 1991, and with the addition of obesity, APACHE-O was defined in 1996. In a metaanalysis study on obesity(BMI>30), the incidence of systemic and local complications were higher[38]. The incidence of mortality is below 4% in patients with an APACHE II score less than 8. The incidence of mortality ranges between 11-18% in patients who have APACHE II scores of 8 or more[39].

Global consensus and a practicable classification system for

Table: Modified Ranson's criteria for acute biliary pancreatitis.

		Acute pancreatitis	Acute biliary pancreatitis
At Admission	Age	Over 55 years	Over 70 years
	WBC	>16.000cells/mm ³	>18.000cells/mm ³
	Blood glucose	>200mg/dl	>220mg/dl
	Serum LDH	>350IU/L	>400IU/L
During initial 48hr	Serum AST	>250U/dl	>250U/dl
	Hematocrit fall	>10 percentage points	>10 percentage points
	BUN increase	>5mg/dl	>2mg/dl
	Serum calcium fall to	<8mg/dl	<8mg/dl
	Arterial pO ₂	<60mmHg	
	Base deficit	>4mEq/L	>5mEq/L
	Fluid sequestration	>6 liters	>4 liters

WBC: White blood cell count, LDH:Lactate dehydrogenase, AST: Aspartate transaminase, BUN: Blood urea nitrogen

acute pancreatitis were offered in the Atlanta Symposium in 1992. This classification provided standardisation in study reporting and communication between clinicians was improved. In time, a revision had been mandatory since some deficiencies were noticed and knowledge about the disease was improved. Atlanta criteria were renewed in 2013.This revision is not intended to be a management guideline. [40].

According to the Atlanta criteria which were defined in 1992, the presence of one or more of the following indicates that acute pancreatitis will have a severe course[41]:1-A Ranson score of 3 or high levels in the first 48 hours. 2-APACHE II score of 8 or higher at any given time.3-Single or multiple organ failure. 4-Single or multiple local complication(necrosis, pseudocyste, abcess).The main changes in the recent Atlanta criteria are:there are two phases of acute pancreatitis in the revised classification, early and late. Severity is classified as mild, moderate or severe. Mild acute pancreatitis which is also the most common form is without any organ failure, local or systemic complications and usually resolves in a week. Presence of transient organ failure, local complications or exacerbation of co-morbid disease is the main considerations of moderately severe acute pancreatitis. Severe acute pancreatitis is described by persistent organ failure (more than 48 hours). Peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst and walled-off necrosis (sterile or infected) are the local complications. Standardised template for reporting CT images is also described[40].

BISAP;a scoring system consisting of five parameters stated below and which gained prospective value in the recent years[42]:BUN >25 mg/dl, altered mental status, SIRS, age>60, pleural effusion.

Balthazar classification

CT and especially dynamic contrast CT gives valuable information about disease severity and prognosis in acute pancreatitis. Balthazar classification which is based CT results was defined in 1985[32].This classification includes the degree of pancreatic enlargement and inflammation severity, presence and amount of fluid collection and the degree of pancreatic necrosis.

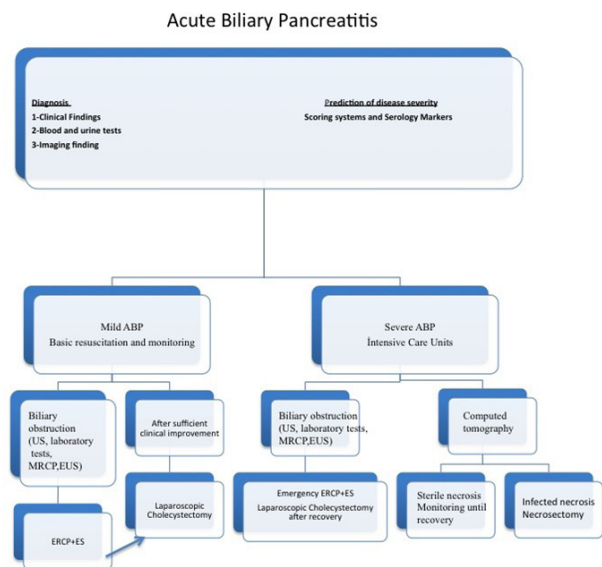
Bank and Agarwal criteria

Researchers like Bank and Agarwal have also identified prognostic systems consisting of different parameters and which are known with their names[44].

Treatment of Acute Biliary Pancreatitis

While most of the attacks in acute pancreatic inflammation are edematous/mild acute pancreatitis that regresses in 5-7 days, necrotizing/severe acute pancreatitis that may lead to mortality may develop in approximately 20% of the cases[45].Therefore, all patients with acute pancreatitis should be hospitalized and given initial supportive care, their disease etiologies should be evaluated and resolved, the severity of pancreatitis should be evaluated, and advanced treatment approach should be planned in accordance with the disease severity(Figure)[7,21,22].

Flowchart for current management of acute biliary pancreatitis.



Abbreviations:ABP:Acute biliary pancreatitisUS:Ultrasonography MRCP: Magnetic resonance cholangiopancreatographyEUS: Endoscopic Ultrasound ERCP: Endoscopic retrograde cholangiopancreatographyES:endoscopicsphincterotomy

Supportive care

In all cases with acute pancreatitis, the initial treatment should include discontinuing oral intake, intravenous fluid replacement and pain management[46].Mild pancreatitis attack rapidly regresses with this treatment, and with regressing abdominal pain, disappearance of nausea and vomiting and normal appetite, oral intake is started again. However, if oral intake does not seem to be possible within 5-7 days, nutritional support should also be added to the treatment[47].

Due to inflammation, there is a significant fluid loss to third spaces such as the interstitial space, and microcirculation is altered as a result of decreasing intravascular volume. This situation both facilitates the development pancreatic necrosis and leads to systemic complications through acute renal failure and the increase in intestinal bacterial translocation[48].Therefore, sufficient fluid and electrolyte replacement play a key role in protection from the systemic complications of acute pancreatitis. Early oxygen support to stabilize arterial oxygen saturation over 95% and fluid resuscitation has been reported to be associated with early regression and mortality in cases of organ failure[49].While the rate of fluid replacement with isotonic-

crystalloids and colloids, when needed, has not been established with clinical studies, the general approach recommends a rate of 250-300cc/hour and a urination rate of 0.5-1.0cc/kg/hour is aimed[50,51].

Nasogastric application is not always necessary, but is suggested in case of bowel obstruction or severe nausea-vomiting. H2 receptor blockers and PPIs should be considered for acute mucosal lesions and gastrointestinal bleedings[45].

Discontinuing oral intake and nutritional treatment

Nutritional support is not necessary as inflammation will be rapidly over in most of the cases. However, if oral intake does not seem to be possible within 5-7 days, enteral nutrition should also be added to the treatment[47]. This situation is frequently observed in patients with severe acute pancreatitis, and especially enteral nutrition started within the first 48 hours of hospitalization has been reported to significantly reduce mortality in severe acute pancreatitis[52]. Medical nutrition is recently understood and has increasing importance in patients with acute pancreatitis. Contrary to previous knowledge, preferring enteral nutrition, rather than parenteral nutrition[18]. Microorganisms infecting the necrotising pancreatitis generally originate from bowel, and are associated with increased bacterial translocation. Therefore, enteral nutrition is the main treatment approach to ensure the integrity of intestinal epithelia, thereby ensuring mucosal barrier integrity to decrease the translocation[53].

Pain management

Pain management is one of the steps in acute pancreatitis treatment. Especially morphine is known to increase oddi sphincter contraction and bupremorphine is recommended in Japanese guidelines, opioid agonist meperidin (petidin) is frequently used for this purpose. Nonsteroid antiinflammatory drugs (NSAIDs), on the other hand, may be used additionally for pain management in cases where narcotics have weak effect or alone in cases with mild symptoms. Albeit, the use of NSAIDs have been reported to reduce the frequency of post-ERCP pancreatitis in patients without oddi sphincter dysfunction, due to antiinflammatory effect[54].

Procedures targeting etiological factor

If cholangitis and extended passage disorder is suspected in patients with ABP, endoscopic retrograde cholangiopancreatography/endoscopic sphincterotomy (ERCP /ES) should be performed in the early stage. If ABP patients have gallstones, it is not recommended to treat bile duct stones with ERCP/ES. Laparoscopic cholecystectomy (LC) is suggested to be performed immediately following disease stabilization. Early cholecystectomy and ERCP reduce the recurrent ABP attacks[55].

LC prevents situations including recurrent ABP, cholelithiasis, choledoch obstruction, cholangitis and biliary cholic. Regarding the timing of cholecystectomy, presence of complications such as severity of pancreatitis, local complications and organ failure, and their resolution is crucial. In the PONCHO study[56], early cholecystectomy performed in the first 72 hours was compared to cholecystectomy with a 25-30 day interval in patients with mild ABP. According to this study, the incidence of readmission and mortality were lower in patients who underwent early cholecystectomy.

Four approaches can be employed to investigate the ABP biliary tract and to treat the gallstones in the main biliary tract: A-ER-

CP/ES can be performed prior to the surgery; after the diagnosis and treatment of gallstones in the main biliary tract. LC should be performed. B-LC and intraoperative cholangiography (IOC), instead of ERCP, can be performed; if a gallstone is detected in the main biliary tract, the procedure can be converted to the open surgery and then choledoch exploration and gallstone treatment can be performed. C- If a gallstone is detected in the main biliary tract using IOC, the procedure can be completed laparoscopically. ES should be performed either during the surgery or in the post-operative phase. D- If a gallstone is detected in the main biliary tract using IOC, choledoch exploration and gallstone treatment can be performed laparoscopically.

Antibiotic treatment and other treatments

Prophylactic antibiotic use is not suggested in cases of mild acute pancreatitis, its use in sterile necrotizing pancreatitis is controversial, because resistant bacterial or fungal infections may develop in prophylactic antibiotic use[57]. On the other hand, the incidence of infected necrosis may reach to 40-70% in patients with necrotizing pancreatitis[58]. As a result of the studies on this topic, 14-day ab initio antibiotic prophylaxis using broad-spectrum carbapenems, which have good penetration into the pancreas, is recommended in cases with pancreatic necrosis rates higher than 30%[18]. If infection is suspected in cases with fever or deterioration of general condition despite antibiotic prophylaxis or if these conditions are observed in the follow-ups, bacteriological examination should be performed using pancreatic thin needle aspiration and surgical debridement should not be delayed when needed[18,58].

In most studies, the use of gabexatemesilate in acute pancreatitis did not decrease the frequency of surgical intervention and mortality, but reduced the frequency of complications[59]. In another study, a reduction in complication frequency and mortality rates has been reported after a 7-day infusion treatment with 2400mg/day dose of gabexatemesilate[60]. Hence, the use of protease inhibitors in severe acute pancreatitis is currently controversial.

While the ability of somatostatin and its analog octreotide to suppress the exocrine secretions of the pancreas, and therefore rest the inflamed pancreatic tissue has caused therapeutic expectations, their efficiency was not demonstrated except for a single study[61,62]. Somatostatin and octreotide have been reported to reduce mortality only in severe acute pancreatitis in a single meta analysis[63], the current notion does not recommend their use in treatment with respect to cost-effectiveness.

Surgical treatment in acute pancreatitis

The role of surgical treatment in patients with pancreatic necrosis is still controversial. According to international consensus, surgical intervention in acute pancreatitis is only recommended for infected pancreatic necrosis[64-66]. Surgical intervention should aim to remove all pancreatic tissues that cause the release of inflammatory mediators. For this purpose, various forms of necrosectomy and drainage methods, including surgical, radiological, endoscopic and minimally invasive, have been defined.

If the patient is clinically stable, surgical intervention is suitable after a 3-4 week of antibiotic therapy, decreased inflammatory reaction and reorganization of the infected region.

Radiological necrosectomy

The method was described by Freeny in 1998, and is based on

the placement of thick percutaneous drainage catheters into the infected pancreatic tissue with the aid of CT. However, it does not result in very successful outcomes, and thus, is recommended for use in removing purulent fluid only in unstable patients in intensive care, and during patient's surgical preparation[67].

Endoscopic necrosectomy

Endoscopic necrosectomy has found increased frequency in the treatment of pancreatic necrosis, fluid collections and pseudocysts, and has considerably high success rates. This technique has gained a place among the natural orifice endoscopic surgery(NOTES)methods. The main advantages of this method include that it does not require general anesthesia, its reproducibility, and it is minimally invasive[68].The major complications are bleeding, free perforation, gastric and duodenal fistules. Endoscopic ultrasonography, doppler imaging and scopy is relatively useful to prevent complications.

Minimally invasive necrosectomy

In recent years, less invasive methods have found a place as an alternative to open surgical interventions, especially in patients who do not have good overall conditions due to organ failure and comorbid diseases[69].In the first method; using percutaneous technique, the necrotic region is reached via nephroscope under CT, necrosectomy is performed, catheters are left for a long period for continuous irrigation, and continuous irrigation is performed with high-volume lavage. In the second method, drains with wide calibration are placed using laparoscopic necrosectomy and direct view[70].

Mild ABP does not leave clinically significant sequel in the long term.The incidence of late-term complications, such as delayed collections, pancreatic pseudocyst, biliary structure, persistent pancreatic fistula, gastrointestinal fistula, incisional hernia, pancreatic exocrine insufficiency and diabetes mellitus, may reach up to 60% in mild ABP.Therefore, long-term follow-up is required to monitor and manage the development of these late complications.

Endoscopic and Interventional Approaches in ABP

The suitable timing of cholecystectomy in ABP depends on the clinical course of the disease.In severe ABP with local and systemic complications, it may be recommended to postpone cholecystectomy after the resolution of these complications. The timing of cholecystectomy in mild ABPs which do not have local and systemic complications is controversial. While some studies recommend it at the time of admission [70,72],others recommend it two, three or four weeks after discharge from the hospital[72-74].

Other strategies, in addition to general precautions and medical treatment, are needed to improve the prognosis. Endoscopic treatment is one of these strategies. However, there is an ongoing discussion on the effect of early ERCP, which is performed between 24-72 hours, and sphincterotomy on the prognosis in cases with ABP[75]. Two metaanalysis on this topic have been published. One of these metaanalyses concluded that early ERCP had no positive effect on complication and mortality in mild or severe pancreatitis, whereas the other metaanalysis-concluded that early ERCP and sphincterotomy reduced complications rates in severe pancreatitis[76,77].The latest study on this topic belongs to the Netherlands acute pancreatitis research group[78].In this prospective, controlled study with 153

cases, the incidence of complications were lower in patients who had severe ABP and cholestasis(bilirubin>2.3 mg/dl and/or diameter of the common bile duct>8 mm) and who underwent early ERCP and sphincterotomy[5].In acute pancreatitis cases without cholestasis, the incidence of complications was similar between patients who received conservative treatment and patients who underwent ERCP. Common bile duct stoneshave been detected in approximately 50% of the cases with/without cholestasis, and similar incidence rates have been determined. In a study by Yeung et al., which involved 172 patients, routine ERCP was not suggested for mild ABP patients[79].

Early ERCP and sphincterotomy may reduce severe pancreatitis-dependent complication rates in selected cases. For the moment, ERCP and sphincterotomy should be recommended for cases with cholangitis, mild or severe pancreatitis with common bile duct stones determined by non-invasive methods, and severe pancreatitis with cholestasis findings, which do or do not have common bile duct stones. Differential diagnosis of cholangitis and pancreatitis can be difficult in patients who have severe pancreatitis and SIRS. In these patients, every effort including methods such as MRCP and EUS should be performed to demonstrate biliary obstruction before ERCP[80].First MRCP, and then EUS[81]can be performed to choose patients for ERCP[82,83].Pancreas, axtrahepatic biliary tracts and ampullary region can be evaluated in detail using EUS[81].

When bilayer drainage cannot be performed using ERCP/ES, endoscopic nasobiliary drainage or percutaneous transhepatic gallbladder drainage procedures can be performed alternatively[22].

In conclusion, the pathogenesis of ABP has not been fully elucidated and several theories have been suggested. Novel laboratory methods and scoring systems have been suggested for both diagnosis and to predict disease severity, and research on these topics is still in progress. Novel therapeutic approaches are also suggested with technological developments.

Competing interests

The authors declare that they have no competing interests.

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